Tetrahedron Letters, Vol.22, No.41, pp 4061 - 4064, 1981
Printed in Great Britain

0040-4039/81/414061-04$02.00/0

STRUCTURES OF TWO RARE IRIDOID GLUCOSIDES FROM *PENSTEMON BARBATUS*

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Summary - The structures of penstemonoside and penstemoside are described.

The natural C(4)-CO_2Me iridoid glucosides with an α-CH_3- and a β-OH functions at C(8) are abundant[2] while it's C(8)-desoxy counterpart, postulated to be the biogenetic percursor of the former[3], has been reported rarely in the literature[4a,b]. This paper describes the structures of two such iridoid glucosides, named penstemonoside (1) and penstemoside (2), isolated from *Penstemon barbatus* (Cav.) Nutt. (Scrophulariaceae).

Penstemonoside (1), $C_{17}H_{26}O_{10}$, $[\alpha]_D^{20}$= -140.20 (c= 0.55, MeOH), was obtained as an amorphous powder. The spectral properties of the compound revealed the presence of an α,β-unsaturated ester [λ_{max} (MeOH): 232 nm (log ε = 4.02); ν_{max} (KBr): 1690 and 1635 cm^{-1}; δ (D_2O): 4.18 (3 H, s, CO_2Me) and 7.90 (1 H, d, J= ~1 Hz, H-C(3))], characteristic of C(4)-CO_2Me iridoids. The ^{1}H-NMR (100 MHz), additionally, showed signals due to a secondary methyl [δ: 1.46 (3 H, d, J= 7 Hz, 3 H-C(10))] and two hemiacetalic protons at δ 6.0 and δ 5.18[5], assignable to H-C(1) and H-C(1'). The large coupling constant ($J_{1'/2'}$= 7 Hz) proves the β-configuration of the anomeric glucose proton.

Acetylation of 1 provided the pentaacetate 1a, $C_{27}H_{36}O_{15}$ (M^+, 600), $[\alpha]_D^{20}$= -133.14 (c= 0.78, $CHCl_3$); ^{1}H-NMR ($CDCl_3$), δ 1.9-2.08 (15 H, 5x OAc), accounting for four hydroxyl functions associated with the glucose moiety and one with the aglucone.

The ^{13}C-NMR spectrum of 1 displayed signals for 17 carbon atoms and is consistent with a C(4)-CO_2Me iridoid glucoside structure[6,7]. The assignment (Table 1) is based on (i) multiplicity of the signals in the SFORD spectrum and (ii) the published ^{13}C-NMR data on this class of compounds.[6,7] These data support the proposed structure for penstemonoside (disregarding the stereochemistry of the aglucone moiety and the location of the hydroxyl function).

The configuration of the methyl and the hydroxyl as well as the placement of the latter at C(6) in 1 are solved by comparing the ^{13}C-NMR spectrum of 1 with related compounds[7]. The appearence of the methyl signal at 16.66 ppm corroborates the presence of an α-methyl at C(10) and the lack of a hydroxy function at C(7)[4c,8]. From the ^{13}C-NMR spectrum of 1 the signals due to the glucose

carbons can easily be discerned and the extra oxygenated carbon signal (cf Table), appearing as a doublet in the SFORD spectrum can be placed only at C(6). Considering the γ- and δ-effects[9] on the carbons C(4) and C(3), respectively, the β-nature of the C(6)-OH can be proposed[10]. On the basis of the above data the structure of penstemonoside is designated by 1.

Penstemoside (2), $[\alpha]_D^{20}$= -100.0 (c= 0.72, MeOH) was also obtained as an amorphous substance. The compound was found to possess the composition $C_{17}H_{26}O_{11}$, one oxygen atom more that penstemonoside (1). The UV spectrum λ_{max}(MeOH): 234 nm (log ε 4.01), the IR spectrum (KBr): 1690 and 1630 cm^{-1} and the ^{1}H-NMR spectrum: δ (D_2O): 4.17 (3 H, s, CO_2Me), 8.06 (1 H, s, H-C(3)) and 1.34 (3 H, d, J= 7 Hz, 3 H-C(10)) showed that penstemoside, like penstemonoside, also has an α,β-unsaturated ester function.

Compound 2 afforded a pentaacetate, $C_{27}H_{36}O_{16}$ (M^+, 616), $[\alpha]_D^{20}$= -105.14 (c= 0.92, $CHCl_3$), in which one hydroxy group remained unaffected (IR and ^{1}H-NMR) indicating it's tertiary nature.

The ^{13}C-NMR (Table) and the ^{1}H-NMR (100 MHz) indicated that penstemoside can be designated as 5-hydroxy penstemonoside. This assignment is based on the following observations: (i) The ^{13}C-NMR spectrum of 2 displayed a singlet (SFORD) at 73.43 ppm accompanied by significant downfield shifts at C(3), C(4) and C(9) and a highfield shift at C(6) as compared to 1. (ii) The ^{1}H-NMR spectra of 2 and it's pentaacetate 2a showed signals at δ 3.1 (1 H, dd, unresolved, H-C(9)) and 2.7 (1 H, dd, unresolved, H-C(9)), respectively. Additionally 2a showed a singlet at δ 3.32 (exchangeable with D_2O) due to a tertiary hydroxyl function. (iii) Finally compound 2 on treatment with acetone-perchloric acid afforded an acetonide[11], characterized by its tetraacetate 2b (^{1}H-NMR, MS). This established the cis-diol function at C(5) and C(6) in 2. The above data can only be satisfactorily explained with structure 2 for penstemoside.

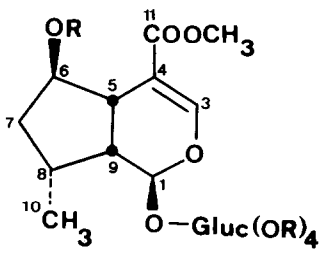
In addition to 1 and 2, we have also isolated the four known iridoids catalpol, globularin, globularicisin and scutellarioside II.

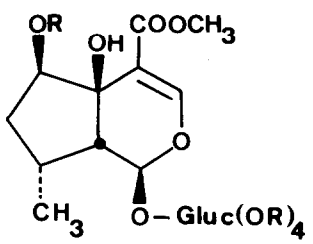
Acknowledgements – This work was supported by research grants of the Swiss Federal Institute of Technology (ETH) and the Swiss National Science Foundation. The authors wish to thank Dr. I. de Mendoza-Heuer, botancial garden, University of Zurich, for confirming the identity of the plant material and Miss. J. Kyzintas for secretarial help.

Table. ^{13}C-NMR Spectral Data of Penstemonoside (1) and Penstemoside (2)

C-Atom	1	2	C-Atom	1	2
1	96.11	95.74	1'	99.66	99.65
3	153.70	155.25	2'	74.50	74.12
4	111.04	113.23	3'	78.12[b]	78.13[b]
5	43.04[a]	73.43	4'	71.51	71.48
6	77.83[b]	76.56	5'	77.83[b]	77.17[b]
7	41.74	40.45	6'	62.74	62.68
8	33.81	31.29	OCH_3	51.82	51.85
9	42.51[a]	50.28			
10	16.66	16.61			
11	169.46	168.13			

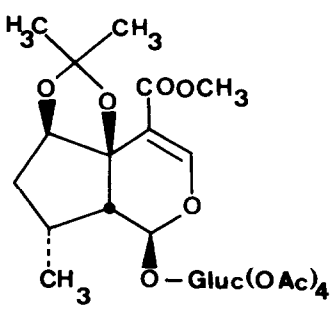
The chemical shifts are given in ppm downfield from TMS (δ TMS = 0).
All compounds are recorded in CD_3OD.
Values with same superscript in the vertical column are interchangeable.





1. Penstemonoside: R = H
1a. Penstemonoside pentaacetate: R = Ac

2. Penstemoside: R = H
2a: Penstemoside pentaacetate: R = Ac



2b

References and Notes

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[9] The averaged chemical shift values for C(4) and C(3) are 113.2 and 152.3 ppm, respectively as calculated from ref. 7. Thus the γ-& δ- effects on C(4) and C(3) in 1 are +2.1 and -1.4 ppm, respectively.

[10] We previously reported (ref. 7) the chemical shift differences between the C(6)-epimers. The present data can now be used to determine the configuration of C(6)-OH more easily even with a single epimer.

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(Received in Germany 5 June 1981)